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Leading a new era of precision oncology

Oncofocus®

Precision Oncology

ONCOFOCUS® TEST REPORT

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Patient demographics

ONC19			
Surname		**Requester**	
Forename		**Contact details**	
DOB		**Date requested**	
Gender			
Histology #		**Tumour %**	
Primary site	Right Lung	**Tumour %**	
Tumour subtype	Small Cell Lung Carcinoma	**(macrodissected)**	35-40%
Tissue Type	Right Lung Biopsy		-

Comment

The DNA extracted from this sample was of optimal quality. The Oncofocus assay on which the sample was run met all assay specific quality metrics for DNA. Unfortunately the RNA extracted from this sample did not pass quality control checks and therefore could not be analysed. Additional material has been requested to complete RNA analysis.

Oncofocus currently targets 505 genes covering oncogenes, fusion genes, genes susceptible to copy number variation and tumour suppressors. Actionable genetic variants detected by Oncofocus are currently linked to 764 anti-cancer targeted therapies/ therapy combinations.

The clinically significant bio-markers identified in this case are summarised on page 2

Within the 'Current Clinical Trials Information' section of this report, starting on page 7, the NCT numbers are hyperlinks to the clinicaltrials.gov webpages which should be accessed to gain further trial specific information

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Clinically Significant Biomarkers

Indicated **Contraindicated**

Genomic Alteration	Copy number	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
AKT1 amplification	6	Clinical trials and/or off-label	Clinical trials and/or off-label	8
TSC2 deletion	0.22	Clinical trials and/or off-label	Clinical trials and/or off-label	7
FANCD2 deletion	0	Clinical trials and/or off-label	Clinical trials and/or off-label	5
RAD50 deletion	0.62	Clinical trials and/or off-label	Clinical trials and/or off-label	4
NTRK1 amplification	7.19	Clinical trials and/or off-label	Clinical trials and/or off-label	3
SETD2 deletion	0	Clinical trials and/or off-label	Clinical trials and/or off-label	3
BAP1 deletion	0	Clinical trials and/or off-label	Clinical trials and/or off-label	3

Sources included in relevant therapies: EMA[1], FDA[2], ESMO, NCCN

Hotspot variants with >10% alternate allele reads are classified as 'detected' with an assay sensitivity and positive predictive value(PPV) of 99%. Copy number variants; amplifications of CN> 6 with the 5% confidence value of ≥4 after normalization and deletions with 95% CI ≤1 are classified as present when the tumour% >50% with a sensitivity of 80% and PPV 100%. Gene Fusions are reported when occurring in >40 counts and meeting the thresholds of assay specific internal RNA quality control with a sensitivity of 92% and PPV of 99%.Other mutations, copy number variations, or fusions that were detected but not classified by the Oncofocus Test as actionable by a known therapeutic targeted agent are not listed in the results section of this report. Supplementary technical information is available upon request.

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Biomarker Descriptions

AKT1 (AKT serine/threonine kinase 1)

Background: The AKT1 gene encodes Protein Kinase B, a serine/threonine kinase, that belongs to a family of closely related protein kinases that also includes AKT2 and AKT3. Growth factor signaling leads to the activation of phosphatidylinositol 3-kinase (PI3K), recruitment of AKT to the plasma membrane, and subsequent activation of downstream effectors including MTOR. The PI3K/AKT/MTOR pathway is central to the regulation of cancer cell proliferation, survival, and metabolism[1,2].

Alterations and prevalence: AKT1 encodes a proto-oncogene that is the target of recurrent somatic mutations in cancer[3]. The most common recurrent mutation is E17K, which is located in the N-terminal pleckstrin homology (PH) domain. E17K is a gain-of-function activating mutation that constitutively targets AKT1 to the plasma membrane and leads to downstream signaling[4,5]. Other recurrent activating mutations include L52H, Q79K, and D323Y/G/N, which disrupt negative regulatory interactions between the PH domain and the kinase domain[6]. AKT1 mutations in cancer are common in breast and endometrial cancers, where they occur at a prevalence of 2-5%[7]. AKT1 mutations are observed at a prevalence of 1-2% in bladder, colorectal, melanoma, and thyroid cancers[7,8]. AKT1 is overexpressed via gene amplification in ovarian cancer, lung squamous cell cancer, and sarcoma at a prevalence of 2-5%[7,8].

Potential clinical relevance: Currently no therapies are approved for AKT1 aberrations. However, in the phase II NCI-MATCH trial, the pan-AKT inhibitor capivasertib (AZD5363) demonstrated a partial response in 23% (8/35) of AKT1 E17K mutated solid tumor patients[9]. Results from a phase I clinical trial of capivasertib demonstrated partial responses in 9/52 heavily pre-treated patients with AKT1 E17K mutated solid tumors, with a median progression-free survival (PFS) of 5.5 months in ER positive breast cancer, 6.6 months in gynecologic cancers, and 4.2 months in other solid tumors[10]. In the same phase I study, an ovarian cancer patient with an AKT1 Q79K mutation demonstrated stable disease lasting 14 months[10].

NTRK1 (neurotrophic receptor tyrosine kinase 1)

Background: The NTRK genes encode a family of neurotrophic receptor tyrosine kinases that function as receptors for nerve growth factors. NTRKs are activated by different neurotrophins and are important for the development of the nervous system[11]. The NTRK1,2,3 proteins are also known as tropomyosin related kinases (TrkA,B,C) because NTRK1 was originally discovered as part of a chimeric fusion gene with tropomyosin-3 isolated from a human colon carcinoma cell line[12]. NTRKs are the target of recurrent chromosomal rearrangements that generate fusion proteins containing the intact tyrosine kinase domain combined with numerous fusion partner genes[13,14]. NTRK fusion kinases are constitutively active and lead to increased RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, or PLCγ/PKC pathway signaling and can promote cell growth and proliferation[13,15].

Alterations and prevalence: NTRK fusions are infrequently observed in diverse cancer types including glioma, glioblastoma, lung adenocarcinoma, colorectal carcinoma, thyroid cancer, and sarcoma[7,13,16,17,18]. In certain cancer subtypes, including infantile fibrosarcoma, papillary thyroid carcinoma, and secretory carcinoma of the breast or salivary gland, NTRK fusions are more prevalent[13,19,20,21].

Potential clinical relevance: The selective tropomyosin receptor kinase inhibitor, larotrectinib[22], was approved (2018) for the treatment of patients with any solid tumors harboring NTRK gene fusions and is the first approved small molecule inhibitor with tissue agnostic indication. The small molecule kinase inhibitor, entrectinib, was granted priority review (2019) by the FDA for NTRK fusion-positive solid tumors as well as ROS1-positive NSCLC. Acquired resistance to first-generation NTRK inhibition is mediated by the acquisition of solvent-front and gatekeeper mutations in the kinase domain. Second-generation NTRK inhibitors have entered development to address these mechanisms of resistance[23,24].

Tier Criteria Met

Genomic Alteration	Tier Classification for Small Cell Lung Cancer
AKT1 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
TSC2 deletion Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
FANCD2 deletion Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
RAD50 deletion Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
NTRK1 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
SETD2 deletion Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials
BAP1 deletion Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials

Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

AKT1 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
capivasertib + olaparib	✖	✖	✖	✖	● (II)
everolimus	✖	✖	✖	✖	● (II)
gedatolisib	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
atezolizumab + ipatasertib	✖	✖	✖	✖	● (I/II)
ARQ-751	✖	✖	✖	✖	● (I)
gedatolisib + palbociclib	✖	✖	✖	✖	● (I)
palbociclib + pictilisib, palbociclib + taselisib	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

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Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

TSC2 deletion

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
capivasertib + olaparib	✖	✖	✖	✖	● (II)
everolimus	✖	✖	✖	✖	● (II)
gedatolisib	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
atezolizumab + ipatasertib	✖	✖	✖	✖	● (I/II)
gedatolisib + palbociclib	✖	✖	✖	✖	● (I)
palbociclib + pictilisib, palbociclib + taselisib	✖	✖	✖	✖	● (I)

FANCD2 deletion

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
durvalumab + olaparib	✖	✖	✖	✖	● (II)
prexasertib	✖	✖	✖	✖	● (II)
talazoparib	✖	✖	✖	✖	● (II)
BAY-1895344	✖	✖	✖	✖	● (I/II)
PNT-737 + chemotherapy	✖	✖	✖	✖	● (I/II)

RAD50 deletion

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
talazoparib	✖	✖	✖	✖	● (II)
BAY-1895344	✖	✖	✖	✖	● (I/II)
PNT-737 + chemotherapy	✖	✖	✖	✖	● (I/II)
pamiparib + tislelizumab	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

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Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

NTRK1 amplification

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
LOXO-195	✖	✖	✖	✖	● (I/II)
sitravatinib	✖	✖	✖	✖	● (I)
VMD-928	✖	✖	✖	✖	● (I)

SETD2 deletion

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
adavosertib	✖	✖	✖	✖	● (II)
BAY-1895344	✖	✖	✖	✖	● (I/II)
PNT-737 + chemotherapy	✖	✖	✖	✖	● (I/II)

BAP1 deletion

Relevant Therapy	EMA	FDA	ESMO	NCCN	Clinical Trials*
durvalumab + olaparib	✖	✖	✖	✖	● (II)
BAY-1895344	✖	✖	✖	✖	● (I/II)
PNT-737 + chemotherapy	✖	✖	✖	✖	● (I/II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Details

Current Clinical Trials Information

Clinical Trials information is current as of 2019-03-01. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers'.

AKT1 amplification

No NCT ID - see other identifier(s)
Phase II Study of Gedatolisib in Advanced Recurrent Small-Cell Lung Cancer Patients Harboring Molecular Alterations in PI3K/AKT/mTOR Pathway (EAGLE-PAT)

Cancer type: Small Cell Lung Cancer

Variant class: AKT1 aberration

Other identifiers: EAGLE-PAT, UMIN000020585

Population segments: Extensive, Second line or greater/Refractory/Relapsed

Exclusion criteria variant classes: BRAF V600E mutation, KRAS activating mutation

Phase: II

Therapy: gedatolisib

Location: Japan

NCT02029001
A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment

Cancer type: Unspecified Solid Tumor

Variant class: AKT1 amplification

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: everolimus

Location: France

NCT03297606
Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: AKT1 aberration

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapy: temsirolimus

Location: Canada

AKT1 amplification (continued)

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD6738 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: 1508016363, 16-314, NCI-2016-00922, OLAPCO, VICCMD1672

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: capivasertib + olaparib

Location: United States

US States: CT, MA, OH, TN

Contact: Manuel Avedissian [203-737-3669; manuel.avedissian@yale.edu]

NCT03673787
Ice-CAP: A Phase I Trial of Ipatasertib in Combination With Atezolizumab in Patients With Advanced Solid Tumours With PI3K Pathway Hyperactivation

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: CCR4720, EudraCT Number: 2017-003005-18, Ice-CAP, IceCAP, IRAS ID 233461

Population segments: Hormone refractory, Second line, Stage III, Stage IV

Phase: I/II

Therapy: atezolizumab + ipatasertib

Location: United Kingdom

NCT02761694
A Phase I Dose Escalation Study of ARQ 751 in Adult Subjects With Advanced Solid Tumors With AKT1, 2, 3 Genetic Alterations, Activating PI3K Mutations, PTEN-null, or Other Known Actionable PTEN Mutations

Cancer type: Unspecified Solid Tumor

Variant class: AKT1 aberration

Other identifiers: 2016-0212, ARQ 751-101, NCI-2016-00913, PTEN-null

Population segments: Estrogen receptor positive, HER2 negative, Progesterone receptor positive, Second line, Stage III, Stage IV

Phase: I

Therapy: ARQ-751

Location: United States

US States: TN, TX

Contact: ArQule [781-994-0300; ClinicalTrials@arqule.com]

AKT1 amplification (continued)

NCT03065062
Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: 16-499, NCI-2017-00434

Population segments: Second line, Squamous Cell, Stage III, Stage IV

Phase: I

Therapy: gedatolisib + palbociclib

Location: United States

US State: MA

Contact: Dr. Nicole Chau [617-632-3090]

NCT02389842
PIPA: A Phase Ib Study to Assess the Safety, Tolerability and Efficacy of the PI3K Inhibitors, Taselisib (GDC-0032) or Pictilisib (GDC-0941), in Combination With PAlbociclib, With the Subsequent Addition of Fulvestrant in PIK3CA-mutant Breast Cancers

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: CCR4191, EudraCT Number: 2014-002658-37, IRAS ID:159997, PIPA

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 negative, HER2 positive, KRAS, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapies: palbociclib + pictilisib, palbociclib + taselisib

Location: United Kingdom

TSC2 deletion

No NCT ID - see other identifier(s)
Phase II Study of Gedatolisib in Advanced Recurrent Small-Cell Lung Cancer Patients Harboring Molecular Alterations in PI3K/AKT/mTOR Pathway (EAGLE-PAT)

Cancer type: Small Cell Lung Cancer

Variant class: TSC2 aberration

Other identifiers: EAGLE-PAT, UMIN000020585

Population segments: Extensive, Second line or greater/Refractory/Relapsed

Exclusion criteria variant classes: BRAF V600E mutation, KRAS activating mutation

Phase: II

Therapy: gedatolisib

Location: Japan

TSC2 deletion (continued)

NCT02029001
A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment

Cancer type: Unspecified Solid Tumor

Variant class: TSC2 deletion

Other identifiers: ET12-081, EudraCT number: 2012-004510-34, MOST, ProfiLER

Population segments: Maintenance/Consolidation, Second line, Stage III, Stage IV, Third line

Phase: II

Therapy: everolimus

Location: France

NCT03297606
Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial

Cancer type: Unspecified Solid Tumor

Variant class: TSC2 aberration

Other identifiers: CA209-9DL, CAPTUR, ESR-17-12831, ML39800, PM1, WI233446

Population segments: Aggressive, Diffuse large B-cell lymphoma (DLBCL), Extranodal marginal zone B-cell lymphoma (MALT), First line, Follicular lymphoma (FL), Indolent, Lymphoblastic lymphoma (LBL), Mantle cell lymphoma (MCL), Other subtype, Second line, Stage III, Stage IV, Waldenstrom's macroglobulinemia (WM)

Phase: II

Therapy: temsirolimus

Location: Canada

NCT02576444
A Phase II Study of the PARP Inhibitor Olaparib (AZD2281) Alone and in Combination With AZD1775, AZD5363, or AZD6738 in Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: 1508016363, 16-314, NCI-2016-00922, OLAPCO, VICCMD1672

Population segments: First line, Second line, Stage IV

Phase: II

Therapy: capivasertib + olaparib

Location: United States

US States: CT, MA, OH, TN

Contact: Manuel Avedissian [203-737-3669; manuel.avedissian@yale.edu]

TSC2 deletion (continued)

NCT03673787
Ice-CAP: A Phase I Trial of Ipatasertib in Combination With Atezolizumab in Patients With Advanced Solid Tumours With PI3K Pathway Hyperactivation

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: CCR4720, EudraCT Number: 2017-003005-18, Ice-CAP, IceCAP, IRAS ID 233461

Population segments: Hormone refractory, Second line, Stage III, Stage IV

Phase: I/II

Therapy: atezolizumab + ipatasertib

Location: United Kingdom

NCT03065062
Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: 16-499, NCI-2017-00434

Population segments: Second line, Squamous Cell, Stage III, Stage IV

Phase: I

Therapy: gedatolisib + palbociclib

Location: United States

US State: MA

Contact: Dr. Nicole Chau [617-632-3090]

NCT02389842
PIPA: A Phase Ib Study to Assess the Safety, Tolerability and Efficacy of the PI3K Inhibitors, Taselisib (GDC-0032) or Pictilisib (GDC-0941), in Combination With PAlbociclib, With the Subsequent Addition of Fulvestrant in PIK3CA-mutant Breast Cancers

Cancer type: Unspecified Solid Tumor

Variant class: PI3K/AKT/MTOR pathway

Other identifiers: CCR4191, EudraCT Number: 2014-002658-37, IRAS ID:159997, PIPA

Population segments: Estrogen receptor positive, Fourth line or greater, HER2 negative, HER2 positive, KRAS, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapies: palbociclib + pictilisib, palbociclib + taselisib

Location: United Kingdom

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FANCD2 deletion

NCT02797977
A Phase I/II Trial of Oral SRA737 (a Chk1 Inhibitor) Given in Combination With Gemcitabine Plus Cisplatin or Gemcitabine Alone in Subjects With Advanced Cancer

Cancer type: Small Cell Lung Cancer

Variant class: DNA repair pathway

Other identifiers: 198606, 30498, CRUKD/16/005, EudraCT Number: 2015-004467-36, PNT737-02, SRA737-02

Population segments: BRCA, Fourth line or greater, KRAS, Pulmonary, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: PNT-737 + chemotherapy

Locations: Spain, United Kingdom

No NCT ID - see other identifier(s)
Single Arm, Open label, Signal Seeking, Phase IIa Trial Of The Activity Of Olaparib In Combination With Durvalumab In Patients With Tumours With Homologous Recombination Repair Defects

Cancer type: Unspecified Solid Tumor

Variant class: FANC deletion

Other identifiers: ACTRN12617001000392, MoST Addendum 3, U1111-1182-6652

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapy: durvalumab + olaparib

Location: Australia

NCT02873975
A Phase II Study of the CHK1 Inhibitor LY2606368 in Patients With Advanced Solid Tumors Exhibiting Replicative Stress or Homologous Recombination Repair Deficiency

Cancer type: Unspecified Solid Tumor

Variant class: Fanconi anemia pathway

Other identifiers: 16-281, I4D-MC-E006, NCI-2016-01564

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapy: prexasertib

Location: United States

US State: MA

Contact: Dr. Geoffrey Shapiro [617-632-4942; Geoffrey_Shapiro@dfci.harvard.edu]

FANCD2 deletion (continued)

NCT02286687
Phase II Study of the PARP Inhibitor BMN 673 (Talazoparib Tosylate) in Advanced Cancer Patients With Somatic Alterations in BRCA1/2, Mutations/Deletions in PTEN or PTEN Loss, a Homologous Recombination Defect, Mutations/ Deletions in Other BRCA Pathway Genes and Germline Mutation in BRCA1/2 (Not Breast or Ovarian Cancer)

Cancer type: Unspecified Cancer

Variant class: Fanconi anemia pathway

Other identifiers: 2013-0961, NCI-2014-02494

Population segments: Fourth line or greater, Stage III, Stage IV

Phase: II

Therapy: talazoparib

Location: United States

US State: TX

Contact: Dr. Sarina Piha-Paul [713-563-1930]

NCT03188965
An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, NCI-2018-00206, Trial ID: 16754

Population segments: Adenocarcinoma, Aggressive, Diffuse large B-cell lymphoma (DLBCL), Hormone refractory, Indolent, Mantle cell lymphoma (MCL), Second line, Squamous Cell, Stage III, Stage IV

Phase: I/II

Therapy: BAY-1895344

Locations: Canada, Singapore, Switzerland, United Kingdom, United States

US State: TX

Contact: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

RAD50 deletion

NCT02797977
A Phase I/II Trial of Oral SRA737 (a Chk1 Inhibitor) Given in Combination With Gemcitabine Plus Cisplatin or Gemcitabine Alone in Subjects With Advanced Cancer

Cancer type: Small Cell Lung Cancer

Variant class: DNA repair pathway

Other identifiers: 198606, 30498, CRUKD/16/005, EudraCT Number: 2015-004467-36, PNT737-02, SRA737-02

Population segments: BRCA, Fourth line or greater, KRAS, Pulmonary, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: PNT-737 + chemotherapy

Locations: Spain, United Kingdom

RAD50 deletion (continued)

NCT02286687
Phase II Study of the PARP Inhibitor BMN 673 (Talazoparib Tosylate) in Advanced Cancer Patients With Somatic Alterations in BRCA1/2, Mutations/Deletions in PTEN or PTEN Loss, a Homologous Recombination Defect, Mutations/ Deletions in Other BRCA Pathway Genes and Germline Mutation in BRCA1/2 (Not Breast or Ovarian Cancer)

Cancer type: Unspecified Cancer

Variant class: RAD50 deletion

Other identifiers: 2013-0961, NCI-2014-02494

Population segments: Fourth line or greater, Stage III, Stage IV

Phase: II

Therapy: talazoparib

Location: United States

US State: TX

Contact: Dr. Sarina Piha-Paul [713-563-1930]

NCT03188965
An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, NCI-2018-00206, Trial ID: 16754

Population segments: Adenocarcinoma, Aggressive, Diffuse large B-cell lymphoma (DLBCL), Hormone refractory, Indolent, Mantle cell lymphoma (MCL), Second line, Squamous Cell, Stage III, Stage IV

Phase: I/II

Therapy: BAY-1895344

Locations: Canada, Singapore, Switzerland, United Kingdom, United States

US State: TX

Contact: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

NCT02660034
A Phase I/Ib, Open Label, Multiple Dose, Dose Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics and Antitumor Activity of the Anti-PD-1 Monoclonal Antibody BGB-A317 in Combination With the PARP Inhibitor BGB-290 in Subjects With Advanced Solid Tumors

Cancer type: Unspecified Solid Tumor

Variant class: HRR pathway

Other identifiers: 16-183, 18-009, A317/290, BGB-A317/BGB-290, BGB-A317/ BGB-290_Study_001, CT783, NCI-2018-00791, P 55217, VICCPHI1814

Population segments: HER2 negative, Pulmonary, Second line, Stage III, Stage IV, Third line, Triple receptor negative

Phase: I

Therapy: pamiparib + tislelizumab

Locations: Australia, France, New Zealand, Spain, United Kingdom, United States

US States: AZ, CA, CO, FL, MA, NY, PA, TN, TX, VA

Contact: Rob Stewart [clinicaltrials@beigene.com]

NTRK1 amplification

NCT03215511
A Phase I/II Study of the TRK Inhibitor LOXO-195 in Adult and Pediatric Subjects With Previously Treated NTRK Fusion Cancers

Cancer type: Unspecified Solid Tumor

Variant class: NTRK aberration

Other identifiers: 17-323, 17-481, 2017-0418, EudraCT Number: 2017-004246-20, LOXO-EXT-17005, NCI-2017-01629

Population segments: Second line, Stage III, Stage IV

Phase: I/II

Therapy: LOXO-195

Locations: Australia, Denmark, France, Republic of Korea, Singapore, Spain, United States

US States: CA, CO, MA, NY, OR, TN, TX, VA, WA

Contact: Patient Advocacy [855-687-5123; clinicaltrials@loxooncology.com]

NCT03556228
An Open-Label, Multiple-Dose, Dose-Escalation Study to Investigate the Safety, Pharmacokinetics, and Pharmacodynamics of VMD-928 in Subjects With Solid Tumors or Lymphoma

Cancer type: Unspecified Solid Tumor

Variant class: NTRK1 amplification

Other identifiers: 18029, VMO-01C

Population segments: Aggressive, Classical, HER2 negative, Indolent, Nodular lymphocyte-predominant, Second line, Stage III, Stage IV, Triple receptor negative

Phase: I

Therapy: VMD-928

Location: United States

US State: CA

Contact: VM Oncology [510-661-6770; om@vmoncology.com]

NCT02219711
A Phase I/Ib Study of MGCD516 in Patients With Advanced Solid Tumor Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: NTRK amplification

Other identifiers: 14-308, 16071502, 2014-1005, 20150094, 516-001, 76853, AAAO0006, NCI-2014-01866, Study 516-001, UMCC 2015.040, USOR Number: 17038, UW15054

Population segments: Adenocarcinoma, EGFR, Hormone refractory, Line of therapy N/A, Second line, Stage III, Stage IV, Third line, Unresectable

Phase: I

Therapy: sitravatinib

Locations: Republic of Korea, United States

US States: AL, CA, CO, FL, IL, LA, MA, MD, MI, NE, NM, NY, OH, PA, SC, TN, TX, UT, VA, WA, WI

Contact: Mirati Therapeutics Study Locator Services [844-893-5530; miratistudylocator@emergingmed.com]

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SETD2 deletion

NCT02797977
A Phase I/II Trial of Oral SRA737 (a Chk1 Inhibitor) Given in Combination With Gemcitabine Plus Cisplatin or Gemcitabine Alone in Subjects With Advanced Cancer

Cancer type: Small Cell Lung Cancer

Variant class: DNA repair pathway

Other identifiers: 198606, 30498, CRUKD/16/005, EudraCT Number: 2015-004467-36, PNT737-02, SRA737-02

Population segments: BRCA, Fourth line or greater, KRAS, Pulmonary, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: PNT-737 + chemotherapy

Locations: Spain, United Kingdom

NCT03284385
A Phase II Study of AZD1775 in SETD2-Deficient Advanced Solid Tumor Malignancies

Cancer type: Unspecified Solid Tumor

Variant class: SETD2 deletion

Other identifiers: 10170, NCI-2017-01670

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapy: adavosertib

Location: United States

US States: CA, DC, MA, MD, MO, PA

Contact: Multiple contacts: See www.clinicaltrials.gov for complete list of contacts.

NCT03188965
An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, NCI-2018-00206, Trial ID: 16754

Population segments: Adenocarcinoma, Aggressive, Diffuse large B-cell lymphoma (DLBCL), Hormone refractory, Indolent, Mantle cell lymphoma (MCL), Second line, Squamous Cell, Stage III, Stage IV

Phase: I/II

Therapy: BAY-1895344

Locations: Canada, Singapore, Switzerland, United Kingdom, United States

US State: TX

Contact: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

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BAP1 deletion

NCT02797977
A Phase I/II Trial of Oral SRA737 (a Chk1 Inhibitor) Given in Combination With Gemcitabine Plus Cisplatin or Gemcitabine Alone in Subjects With Advanced Cancer

Cancer type: Small Cell Lung Cancer

Variant class: DNA repair pathway

Other identifiers: 198606, 30498, CRUKD/16/005, EudraCT Number: 2015-004467-36, PNT737-02, SRA737-02

Population segments: BRCA, Fourth line or greater, KRAS, Pulmonary, Second line, Stage III, Stage IV, Third line

Phase: I/II

Therapy: PNT-737 + chemotherapy

Locations: Spain, United Kingdom

No NCT ID - see other identifier(s)
Single Arm, Open label, Signal Seeking, Phase IIa Trial Of The Activity Of Olaparib In Combination With Durvalumab In Patients With Tumours With Homologous Recombination Repair Defects

Cancer type: Unspecified Solid Tumor

Variant class: BAP1 deletion

Other identifiers: ACTRN12617001000392, MoST Addendum 3, U1111-1182-6652

Population segments: Second line, Stage III, Stage IV

Phase: II

Therapy: durvalumab + olaparib

Location: Australia

NCT03188965
An Open-label, First-in-human, Dose-escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Maximum Tolerated Dose and / or Recommended Phase II Dose of the ATR Inhibitor BAY1895344 in Patients With Advanced Solid Tumors and Lymphomas

Cancer type: Unspecified Solid Tumor

Variant class: DNA repair pathway

Other identifiers: 18594, 2017-0186, BAY1895344/18594, EudraCT Number: 2016-004484-39, IRAS ID-218516, NCI-2018-00206, Trial ID: 16754

Population segments: Adenocarcinoma, Aggressive, Diffuse large B-cell lymphoma (DLBCL), Hormone refractory, Indolent, Mantle cell lymphoma (MCL), Second line, Squamous Cell, Stage III, Stage IV

Phase: I/II

Therapy: BAY-1895344

Locations: Canada, Singapore, Switzerland, United Kingdom, United States

US State: TX

Contact: Bayer Clinical Trials Contact [888-842-2937; clinical-trials-contact@bayer.com]

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Evidence Summary by Variant Class

A variant class hierarchy was created to summarize gene variants with associated clinical evidence. Evidence items refers to citations across the different global data sources.

AKT1 amplification

Variant Class	Evidence Items
PI3K/AKT/MTOR pathway	8
↳ AKT1 aberration	3
↳ AKT1 amplification	1

TSC2 deletion

Variant Class	Evidence Items
PI3K/AKT/MTOR pathway	8
↳ TSC2 aberration	2
↳ TSC2 deletion	1

FANCD2 deletion

Variant Class	Evidence Items
DNA repair pathway	8
↳ DNA repair deletion	0
↳ FANCD2 deletion	0
Fanconi anemia pathway	2
↳ FANC deletion	1
↳ FANCD2 deletion	0

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Evidence Summary by Variant Class (continued)

A variant class hierarchy was created to summarize gene variants with associated clinical evidence. Evidence items refers to citations across the different global data sources.

RAD50 deletion

Variant Class	Evidence Items
DNA repair pathway	8
↳ DNA repair deletion	0
↳ RAD50 deletion	1
HRR pathway	1
↳ RAD50 deletion	1

NTRK1 amplification

Variant Class	Evidence Items
NTRK aberration	1
↳ NTRK amplification	1
↳ NTRK1 amplification	1
↳ NTRK1 aberration	0
↳ NTRK1 amplification	1

SETD2 deletion

Variant Class	Evidence Items
DNA repair pathway	8
↳ DNA repair deletion	0
↳ SETD2 deletion	1

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Evidence Summary by Variant Class (continued)

A variant class hierarchy was created to summarize gene variants with associated clinical evidence. Evidence items refers to citations across the different global data sources.

BAP1 deletion

Variant Class	Evidence Items
DNA repair pathway	8
↳ DNA repair deletion	0
↳ BAP1 deletion	1

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